

# Cigarette Smoking as a risk factor for Opioid Use

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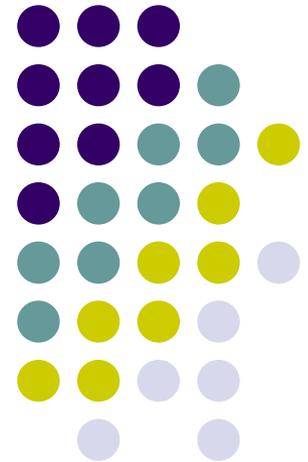


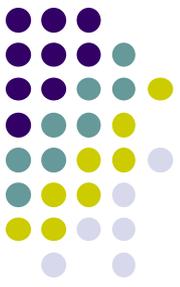
The PRIME Center



Pain Research, Informatics, Multimorbidities, and Education

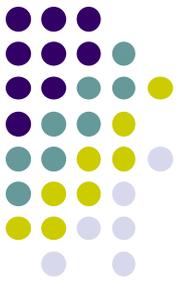
Enhancing Pain Care for Veterans





# Outline

- Provide a brief overview of smoking status and pain intensity
- Describe new research (in press) examining smoking status and opioid use in Veterans
- Examine the role of smoking as a risk factor for opioid use
- Discuss clinical implications and future research

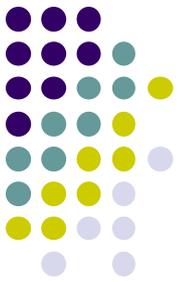


# Poll Question #1

- What is your primary role in VA?
  - Student, trainee, or fellow
  - Clinician
  - Researcher
  - Administrator, manager or policy-maker
  - Other

# Cigarette smoker with pain



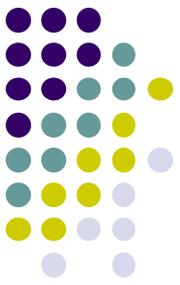


# Prevalence of Smoking

- 17-18% in general population
- 24-42% in patients with chronic pain
- 50-68% of patients in pain treatment programs

Fishbain DA et al. Pain Medicine 2013;14:403-416; Orhurhu VJ. Tobacco induced diseases 2015;13:17

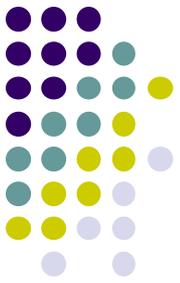
# Smokers with lung cancer report higher pain levels



- We published one of the first studies on smoking and cancer pain
- Surveyed 893 patients with lung cancer
- 41% mod/severe pain intensity ( $\geq 4$ )
- 17% persistent smokers
- Persistent smokers were **1.6 times** more likely to report mod/severe pain intensity compared to non-smokers and former smokers.

Daniel (**Bastian**) et al Journal of Pain 2009;10:323.

# Smokers have more back pain



- Meta-analysis of 40 studies
- Current Smokers had an increased prevalence of low back pain compared to non-smokers OR=**1.30** (95% CI 1.2-1.4)
- Former smokers OR=**1.24** (95% CI 1.1-1.4) had lower odds of back pain

Shiri R et al. Am J Med 2010;123:87e7-87e35

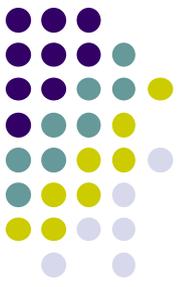
# Heavy smokers report more pain



- 7,124 survey respondents from population database in Germany ages 18-79
- 9% women and 17% men were heavy smokers ( $\geq 20$  cigs/d)
- Heavy smokers report more pain locations and higher pain intensity in past 7 days

John U, et al Prev Med 2006;43:477 & John U, et al Drug Alc Dep 2006;85:49.

# Acute Analgesic effects of Nicotine: Meta Analysis



- Examined 21 tests of pain tolerance and 15 tests of pain threshold in lab studies.
- Nicotine (tobacco smoke and other products) was associated with small analgesic effects.
- Acute nicotine-induced analgesia could make smoking more rewarding and harder to give up suggesting the need for nicotine replacement therapy in smokers with pain when they try to quit smoking.

Ditre JW et al Pain 2016;157:1373-81.

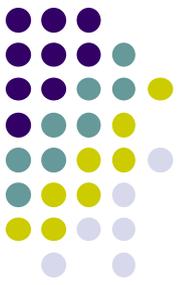
# Bidirectional Feedback Loop



- Does smoking increase pain? Or does pain increase the urge to smoke?
- Drs. Ditre & Brandon have hypothesized a reciprocal relationship between pain and smoking that operates as a positive feedback loop, leading to greater pain intensity, increased smoking, and the maintenance of nicotine dependence and chronic pain

Ditre JW & Brandon TH J Abnorm Psychol 2008;117:467

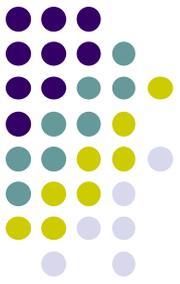
# Smoking and Pain among OEF/OIF Veterans



- 355,966 men and 50,988 women OEF/OIF Veterans with at least one visit from 2001-12
- Mean age 30 years; 37% were current smokers; 16% were former smokers; and 34% reported mod/severe pain intensity ( $\geq 4$ )
- Current smoking **OR=1.25** (95%CI 1.2-1.3)  
Former smoking **OR=1.02** (95%CI 1.01-1.05)  
associated with mod/severe pain intensity adjusting for age, gender, mental health dx.

Volkman, Becker, **Bastian** et al, Pain Medicine 2015; 16:1690-96

# Smoking and Opioid Use among OEF/OIF Veterans



- To determine if smoking status is associated with opioid receipt in OEF/OIF/OND Veterans
- To examine the correlates of smoking and opioid receipt

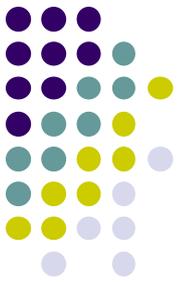
Bastian et al, Pain Medicine 2016; in press



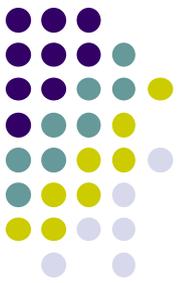
# Study Design

- Cross-sectional analysis of the Women Veteran Cohort Study (WVCS)
- Veterans who had at least one visit to a Veterans Health Administration (VHA) primary clinic between 2001-12
- VHA data and electronic records contained within the Corporate Data Warehouse

# Key Variables

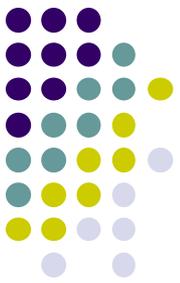


- *Cigarette Smoking Status*: The most recent status of Veterans were categorized as current, former, or never smokers based on a comprehensive algorithm
- *Pain Intensity*: On a 0 (no pain) to 10 (worst pain imaginable) scale, the highest pain intensity score was selected (within +/- 30 days of smoking status)
- *Opioid Receipt*: Defined as at least one filled prescription for opioids in VHA drug class CN101, excluding Buprenorphine, Methadone and Tramadol (within +/- 30 days of smoking status)



# Correlates of Opioid use (8%)

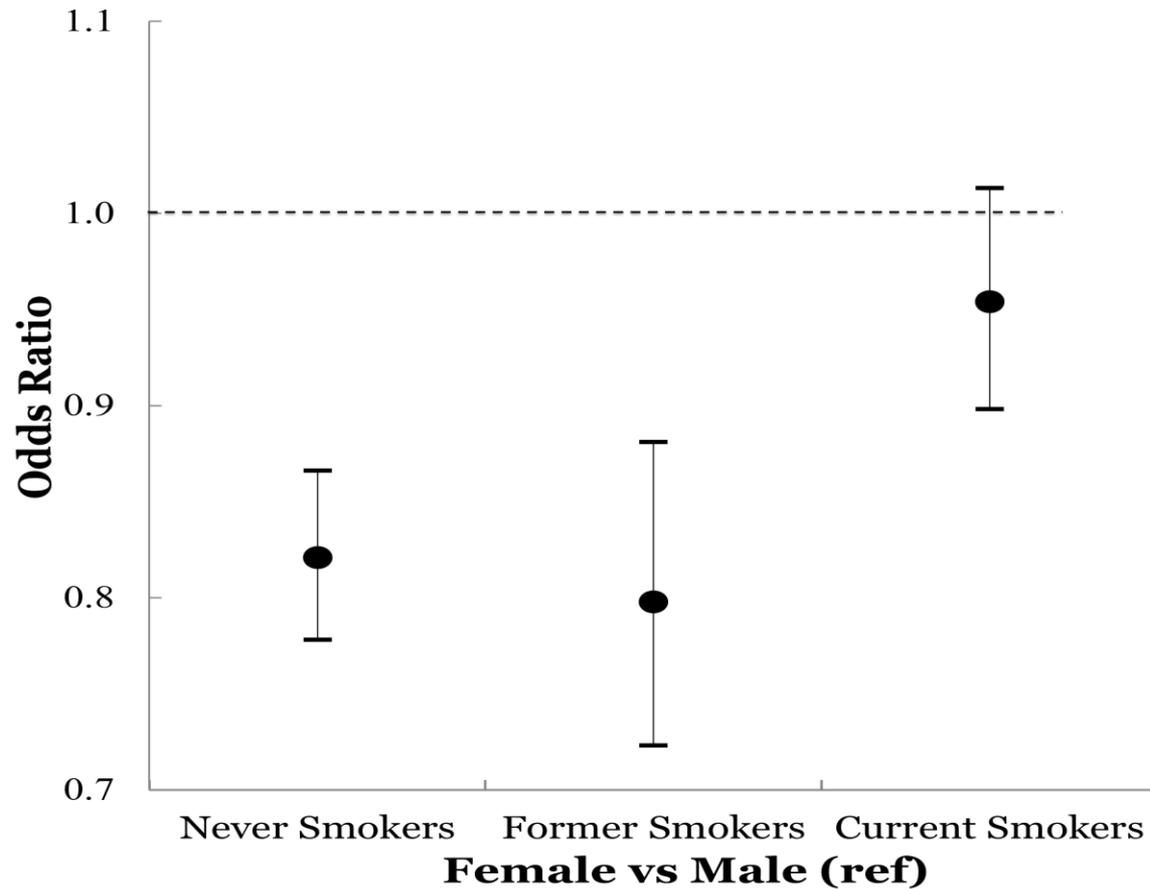
Variables	Total (n=406,954)	Yes (n=32,994)	No (n=373,960)	p-value
<b>Age (mean (SD) median)</b>	30.1 (9.3) 26	29.6 (9.0) 26	30.1 (9.3) 26	<0.0001
<b>Gender (%)</b>				<0.0001
Female	12.5	10.3	12.7	
Male	87.5	89.7	87.3	
<b>Race (%)</b>				<0.0001
White	60.3	65.8	59.8	
Black	15.5	13.2	15.7	
Hispanic	11.2	9.0	11.4	
Other/Unknown	13.0	12.0	13.1	
<b>Service-Connected Disability 50% or &gt; (%)</b>	21.3	43.6	19.3	<0.0001
<b>Pain Intensity (%)</b>				<0.0001
None to mild (0-3)	66.3	22.8	70.1	
Moderate to Severe (4-10)	33.7	77.2	29.9	
<b>Mental Health (%)</b>				
Mood Disorders	9.5	18.6	8.7	<0.0001
PTSD	25.9	47.5	24.0	<0.0001
<b>Smoking Status (%)</b>				<0.0001
Current	37.2	49.1	36.2	
Former	16.0	15.9	16.0	
Never	46.8	35.0	47.8	

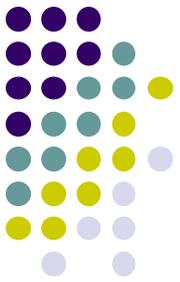


# Logistic models of Opioid use

<b>Variables</b>	<b>Unadjusted Odds Ratio (95% CI)</b>	<b>Adjusted Odds Ratio (95% CI)</b>
Age/per year	0.99 (0.99-1.00)	0.99 (0.98-0.99)
Current Smoker	1.70 (1.66-1.74)	1.56 (1.52-1.61)
Former Smoker	0.99 (0.96-1.03)	1.27 (1.22-1.32)
Male	1.28 (1.23-1.32)	1.16 (1.11-1.20)
Service-connected disability $\geq 50\%$	3.23 (3.16-3.30)	1.98 (1.92-2.03)
Pain Intensity (Moderate-Severe vs None-Mild)	7.98 (7.77-8.19)	6.55 (6.38-6.73)
Mood Disorders	2.41(2.33-2.48)	1.22(1.17-1.25)
PTSD	2.87 (2.81-2.94)	1.44 (1.39-1.48)

# Gender sub-analyses





# Summary of Results

- 8% of Veterans received at least one opioid Rx
- Current and former smoking were associated with higher odds (**1.56 and 1.27**, respectively) of opioid receipt compared to never smoking
- Women (never and former smokers only) were less likely than men to receive an opioid prescription.
- Current smoking women were just as likely as current smoking men to receive an opioid prescription

# Mechanisms for smoking to confer risk for opioid use



- Chronic nicotine exposure may result in dysregulation of the endogenous opioid system, leading to greater pain and cross-tolerance to opioids
- Nicotine may sensitize the neural system to enhance rewarding properties of opioids
- Co-occurring risk factors such as depression and other substance use

Shi Y, Anesthesiology 2010;113:977-992; Vihavainen T Eur J Pharmacol 2008;587:169-74



# Why study opioids?

- Increase in rates of overdose and all-cause mortality
- It could be helpful to predict who is at risk for opioid use
- When examining the literature in this area it is useful to look at any, episodic, or long-term use, and to look at dose (morphine equivalents), abuse and misuse.

# Progression from short-term to episodic or long-term opioid use



- Rochester cohort in Minnesota (n=142,377)
- 293 patients had a new opioid RX in 2009
- 21% progressed to episodic and 6% to long-term use in the subsequent year
- Smokers were **1.85 times** more likely to become episodic or long-term users compared to never smokers

Hooten WM Mayo Clin Proc 2015;90:850-6.

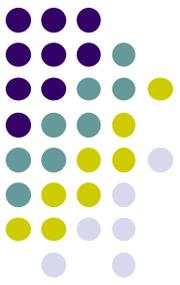


# Opioid use after C-section

- About 1 in 300 opioid naïve women become persistent opioid users following C-section
- Smokers **3 times more likely** to become long-term opioid users
- Other risk factors include: cocaine use, back pain, migraines, antidepressant use, and benzo use.

Bateman BT et al [Am J Obstetrics & Gynecology](#) 2016;215:353.e1-18

# Smoking and prescription opioid use in a pain program



- 1,241 patients enrolled in a pain treatment program
- 25% current smokers
- Smokers had a greater morphine equivalent dose compared to non-smokers
- Multivariable model (adjusting for depression) smoking associated with greater opioid use

Hooten WM et al. Pain 2011; 152:223

# Predictors of discontinuing Long-term Opioids



- 1.9 million Veterans with opioid prescription 2009-2011 and 550,616 met criteria for long-term opioid use
- Factors associated with discontinuing: both younger and older age, lower dosage, less than 90 days prescription in prior year, **not smoking**, mental illness.

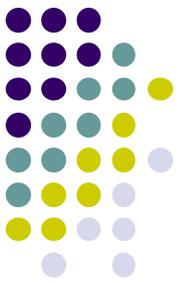
Vanderlip ER et al. Pain 2014;155:2673-79



# Risk factors for opioid abuse

- 694,851 patients in pharmacy database
- 2067 (0.3% with opioid abuse/dependence)
- Looked at risk factors in 12 months prior to opioid RX: younger age, male, chronic opioid use, mental illness, alcohol abuse, high MED, **tobacco use (OR=1.80)**, using multiple pharmacies, and certain geographic regions

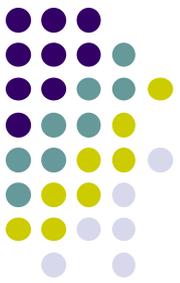
Cieslelski T et al. Am J Med 2016;129:699-705.



# Smoking and Opioid Abuse

- Using admin data, authors identified (n=821,916) patients with 1 or more opioid prescription in 2007-09
- 6,380 were diagnosed with Opioid abuse
- **OR=1.45** for smokers to be diagnosed with opioid abuse compared to non-smokers

Rice JB, Pain Med 2012;13:1162-1173



# Smoking and Opioid misuse

- National Survey on Drug Use and Health (n=24,348)
- Daily smokers were **5 times** more likely to have a diagnosis of opioid abuse and **3 times** more likely to report nonmedical prescription opioid misuse compared to never smokers.
- Heavy smoking was associated with more opioid abuse and misuse.

Zale EL Nicotine & Tob Res 2015;1096-1103



# Poll Question #2

- Challenges to addressing smoking in Veterans with pain (select all that apply):
  - Lack of time in clinic visit
  - Need more evidence that smoking is a risk factor for pain
  - Need more evidence that smoking is a risk factor for opioid use
  - Patients can't or won't quit smoking while they have pain

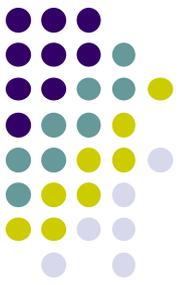
# Attitudes about smoking and pain



- Qualitative study on physician attitudes
- Focus group of 7 physicians (specialists)
- These physicians identified many barriers to smoking counseling in a pain treatment clinic
  - Hard to “zone in on the smoking part”
  - Patients smoke to cope with pain and they are under too much stress to try and quit

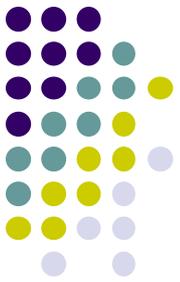
Hooten WM et al Pain Practice 2011;11:552

# CBT for smoking cessation for patients with chronic pain



- 7 session individual and group-based CBT intervention developed for patients in a 3-week hospitalized pain treatment program.
- In pilot RCT, 30% were abstinent at end of intervention compared to 10% in control
- At 6 month follow-up, 20% were abstinent at end of intervention compared to none in control

Hooten WM Addictive Behaviors 2014;39:593-9



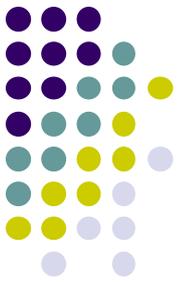
# Future Studies

- Need more RCTs to examine impact of smoking cessation on pain intensity
- VA HSR&D recently awarded us (Becker & Bastian at VA Connecticut) an IIR to compare the effectiveness of a combined smoking cessation/pain CBT intervention to smoking cessation alone in smokers with pain.



# Clinical summary

- Ask about smoking status (including e-cigs) when considering the risks and benefits of prescribing an opioid.
- Given the concerns about potential abuse and misuse, should smokers be given naloxone?
- If smokers with pain are interested in quitting, prescribe nicotine replacement therapy



# Funding and Support

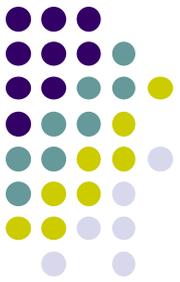
- These analyses were supported by the VA Health Services Research & Development (IIR 12-118, CIN 13-407, and LIPS 96-013)

## The PRIME Center



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# Thank You!

Questions/Comments:

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